12/12

PATENT COOPERATION TREATY

PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/003488	12.08.2004	12.08.2003

International Patent Classification (IPC) or both national classification and IPC
C08B37/00, C07K1/107, A61K47/48

Applicant
LIPOXEN TECHNOLOGIES LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/003488

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/003488

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	14,15
	No:	Claims	1-13,16-22
Inventive step (IS)	Yes:	Claims	
	No:	Claims	14,15
Industrial applicability (IA)	Yes:	Claims	1-22
	No:	Claims	

2. Citations and explanations

see separate sheet

1. Cited literature

(a) The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: US-A-5 329 028

D2: D. Macmillan et al., Chemistry And Biology, Current Biology, London, GB (2001), 8(2), 133-145

D3: Database Derwent WPI; AN: 1980-23224C & **SU-A-675 053**

D4: WO-A-01 87 922

(b) In the following arguments, page or column A, lines B to C will be cited as A/B-C.

2. Novelty

(a) Document **D1** describes the coupling of 4-(4-N-maleimidophenyl)butyric acid hydrazide (MPBH) to the sialic acid residues of soluble CD4 glycoprotein (see 2/14-16; 6/28-33). The sialic acid portion of CD4 is oxidised by means of $NaIO_4$ and the hydrazide group of MPBH reacts with the aldehyde group of the oxidised CD4. The product thus obtained can react with thiol groups of proteins (see 6/28-45 and fig. 1). As an alternative to MPBH, a hydrazide functional pyridyl disulphide is mentioned (see 6/21-26).

Therefore, the subject-matter of **claims 1-13 and 16-22** is not novel.

(b) Document **D4** teaches to oxidise polysialic acid (colominic acid) with periodate in order to convert the terminal -CH(OH)-CH(OH)-CH_2OH group into a -C(H)=O group (see Fig. 1) and to couple this terminal aldehyde group by reductive amination with lysyl units of a protein (see claims 1, 10, 11 and 16; 6/24-7/6, 8/5-15, 10/6-11/2 and example 4).

The product thus formed is one according to present claim 7, alternative ii) where R^1=H, R^2=-NR^6R^7, where R^7=H.

So, the subject-matter of **claims 7 and 8** is also not novel in view of **D4**.

3. Inventive step

(a) Document **D2** discloses in Fig. 1 the reaction of a cysteine unit of a protein with an alpha-iodoacetamido sugar. It is mentioned that this reaction is selective (see p. 134, right col., 2nd para.).

(b) It was quite obvious to prepare this alpha-iodoacetamido sugar by condensation of the amino group of the sugar with iodoacetic acid in the presence of a carbodiimide.

For instance **D3** discloses to condense the amino group of methyl(-9-anthryl)-amine with iodoacetic acid in the presence of dicyclohexyl-carbodiimide.

(c) Therefore, it was obvious to modify the process described in **D1** by reacting an amino group of the polysaccharide with iodoacetic acid.

So, the subject-matter of **claims 14 and 15** is not based on an inventive step.

4. Objections under Art. 5 (lack of disclosure) and 6 PCT (support of the claims by the description)

(a) The present description is silent as to how most of the compounds of **claim 7** may be produced.

So, there is no information in the description how the compounds of the alternative I) may be made, i.e. compounds where a group R^3 (i.e. $-CH_2CHR^4R^5$ or $-CH(CH_2OH)CHR^4R^5$) is bonded to a glycosyl group via an oxygen atom.

Likewise, the description does not give any indication as to how compounds of the alternative ii) may be obtained, where R^6 and R^7 together are a 1,3-but-2-enediol group.

(b) Therefore the person skilled in the art is "... unable ... to extend the particular teaching of the description to the whole of the field claimed ..." (see the PCT Guidelines 5.44) so that **claim 7** is not supported by the description, contrary to the requirements of Art. 6 PCT.

(c) In addition to that the description does not - as far as the teaching of claim 7 is concerned - "disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art." (Art. 5 PCT).

5. Clarity of the claims (Art. 6 PCT)

(a) **Claim 1** is unclear. There seems to be at least one word missing in the expression "... comprising a polysaccharide a pendant moiety linked at least one terminal unit ...".

(b) **Claim 7** is unclear since the radical R^3 is not defined in definition ii).

6. The preferred features in **claims 6, 10, 12, 14, 15, and 20** denoted by the word "preferably" represent features that do not limit the claims. They are thus obviously irrelevant (Rule 9.1(iv) PCT) and render these claims inconcise, contrary to the requirements of Article 6 PCT.

7. The last claim should bear the number 22 instead of 20.